## DETAILED ACTION

### Status of Action

Receipt of Application No. 11/581,461 filed on 06/01/2006 is acknowledged. Claims 1-20 are pending in this application.

### Status of Claims

Accordingly, claims 1-20 are presented for examination on the merits for patentability.

### Claim Objection

Claims 1-20 are objected to because of the following informalities: Claims 1 and 7 recite the active agent "venlafaxin", which the proper spelling of this active agent should be venlafaxine". In addition, claim 10 recites the constituent "magnesium state", which should be "magnesium stearate". Appropriate correction is required.

### Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-6, 8-9, 11-20 are rejected 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

applicant regards as the invention. All dependent claims are also included in this rejection.

Claim 1 recites the amounts of venlafaxine from 20-60 % by weight and a water poorly permeable polymer from 1-3 % by weight, which are indefinite because it is unclear whether these amounts are relative to the total amount of the tablet, or they are the amount relative to the core or the coating portion only.

Claims 5-6 and 15-20 contain the trademark/trade name METHOCEL K100 M Premium EP and EUDRAGIT L30 D. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe the hydrophilic polymer and the water-poorly permeable polymer; and, accordingly, the identification/description is indefinite.

Claims 5-6 and 15-20 recite a limitation "wherein the coated tablet comprises 75 mg of the active substance, based on the venlafaxine base", which is indefinite because it is unclear whether Applicants intend to claim an active substance which is different than the venlafaxine compound, or Applicants intend to claim a salt form of venlafaxine

compound. Since one of ordinary skill in the art would not be reasonably apprised what this active substance is; and thus, the claims are rendered indefinite.

In addition, the phrase "the active substance" recites in claims 5-6 and 15-20 lacks sufficient antecedent basis because their preceding claim 1 does not recite a component named "an active substance".

Claim 11 recites a constituent "triethyl citrate", which lacks sufficient antecedent basis because its preceding claim 7 recites the optional component is "acetyl triethyl citrate". Since "triethyl citrate" is not equivalent to "acetyl triethyl citrate"; therefore, the recitation of triethyl citrate in claim 11 lacks sufficient antecedent basis.

## Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham **v.** John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

**(1) Claims 1, 3-6, 8-9, 14, 16-17 and 19-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Janez et al. (WO 03/055475) in view of Fujisawa et al. (U. S. Patent No. 6,114,284).**

**Applicants Claim**

Applicants claim a controlled release coated tablet comprising: (i) venlafaxine in an amount from 20-60 % by weight; (ii) a hydrophilic polymer, in an amount from 30-70 % by weight, in its core; (iii) a water poorly permeable polymer, in an amount from 1-3 % by weight, in its coating; wherein the hydrophilic polymer comprises a cellulose ester, and the water poorly permeable polymer comprises an acrylic polymer.

**Determination of the scope and content of the prior art**

**(MPEP 2141.01)**

Janez et al. teach an improved solid controlled release pharmaceutical formulation, in the form of tablet, comprising venlafaxine and a process for the preparation thereof. Janez et al. teach that the pharmaceutical formulation comprises: (i) a core, which composed of an active drug venlafaxine or its pharmaceutically acceptable salts, and a combination of two hydrophilic polymers having different viscosities; (ii) a polymer coating, which the core is coated with, in an amount from 1-15 % by weight comprising a combination of two polymers having different water permeability (page 2, line 5-20; page 23, claims 1 and 23).

Janez et al. first teach that the amount of venlafaxine in the solid formulation can be present from 10 to 400 mg, i.e. 75 mg or 150 mg (page 6, lines 19-22; page 23, claims 2-7).

Janez et al. next teach that the hydrophilic polymers is a combination of low and high viscosity hydrophilic polymers, which modifies the release of the active substance, i.e. venlafaxine hydrochloride, in such a way that it is sustained over 24 hour period (page 3, lines 3-11; page 4, lines 25-28); wherein the high viscosity hydrophilic polymer can be a hydroxypropylmethyl cellulose (i.e. METHOCEL K100 M Premium) and can be present in an amount from 5-70 % by weight (page 4, lines 29-32; page 5, lines 1-16 and Table; page 13, line 11-12; page 23, claims 8-10); or in an amount of 70 mg, 150 mg or 250 mg in a tablet (see: Examples 1-5).

Janez et al. next teach that one of the polymers of the coating is a water low permeable polymer which is insoluble in water or contains groups permeable for water in a small portion, i.e. methacrylic acid copolymers, low permeable poly(ethylacrylate, methylmethacrylate) trimethylammoniumethylmethacrylate chloride. In addition, Janez et al. teach that the selection of the water low permeable polymer should not be restricted by those examples therein (page 2, lines 28-33; page 7, lines 6-15, 32-34; page 8, lines 1-12; page 25, claims 17-18).

Janez et al. also teach that the core may contain other usual ingredients useful in the preparation of solid pharmaceutical dosage forms, i.e. one or more glidants such as magnesium stearate (page 6, lines 13-14), and the coating may contain one or more

plasticizers such as acetyl triethyl citrate, triethyl citrate; one or more anti-sticking agents such as talc, magnesium stearate (page 9, lines 11-12, 18, 20-21).

Janez et al. further exemplify the composition in the form of tablet, which the table core comprises 169.73 mg of venlafaxine hydrochloride, 250 mg of hydroxypropylmethyl cellulose (METHOCEL K100MP), and magnesium stearate; and the tablet coating comprises 3.5 mg low water permeable coating polymers (EUDRAGIT RL 30D: an aqueous dispersion of poly(ethylacrylate, methylmethacrylate) trimethylammoniumethylmethacrylate chloride, and EUDRAGIT RS 30D: an aqueous dispersion of poly(ethylacrylate, methylmethacrylate) trimethylammoniumethyl-methacrylate chloride); plasticizers triethyl citrate, and talc (page 18-19, Example 4).

**Ascertainment of the difference between the prior art and the claims**

**(MPEP 2141.02)**

Janez et al. do not teach the water low permeable coating polymer, namely EUDRAGIT L30 D, as claimed. However, Janez et al. teach other types of water low permeable acrylic polymers, i.e. EUDRAGIT RL 30D and EUDRAGIT RS 30D, for coating the tablet containing venlafaxine hydrochloride and a hydrophilic polymer (METHOCEL K100MP).

**Finding of prima facie obviousness Rational and Motivation**

**(MPEP 2142-2143)**

It would have been obvious to a person of ordinary skilled in the art at the time the invention was made to follow the teaching of Janez et al. to arrive at the claimed invention.

One of ordinary skill in the art would have been motivated to substitute the acrylic type polymers: EUDRAGIT RL 30D and/or EUDRAGIT RS 30D taught in Janez with another functional and structural equivalent acrylic type polymer, i.e. EUDRAGIT L30 D, because they all are the acrylic type polymers and all have low water permeability; therefore, they can be used interchangeably for coating purposes.

With respect to the recitations where the coated tablet comprises 75 mg of venlafaxine, 100-200 mg of METHOCEL K 100MP and 3-10 mg of EUDRAGIT L30 D-55, although Janez does not exemplify a formulation comprising these constituents: venlafaxine, METHOCEL K 100MP and EUDRAGIT L30 D-55, in said specific amounts; however, Janez suggests that the solid controlled release pharmaceutical formulation comprises a desirable pharmaceutical amount of venlafaxine, i.e. 75 mg or 150 mg; a desirable amount of METHOCEL K100 M Premium, i.e. 70 mg, 150 mg or 250 mg; and a total of 3.5 mg of low water permeable coating polymers (EUDRAGIT RL 30D and EUDRAGIT RS 30D). Therefore, one of ordinary skill in the art when reviewing the reference of Janez would be motivated to try these suggested amounts range, and selects the amount or amount ranges that gives the best, desirable results.

From the teaching of the reference, one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the

invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

**(2) Claims 7 and 10-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Janez et al. (WO 03/055475) in view of Seth, P. (U. S. PG-Pub. No. 2003/0091634).**

**Applicants Claim**

Applicants claim a controlled release coated tablet comprising: (i) venlafaxine in an amount from 20-60 % by weight; (ii) a hydrophilic polymer, in an amount from 30-70 % by weight, in its core; (iii) a water poorly permeable polymer, in an amount from 1-3 % by weight, in its coating. Applicants also claim a process of making the coated tablet set forth above.

**Determination of the scope and content of the prior art**

**(MPEP 2141.01)**

The teaching of Janez et al. has been set forth above. In addition, Janez et al. also teach a process of making the tablet, wherein the active substance venlafaxine, the hydrophilic polymers, and other usual adjuvants useful in the preparation of solid pharmaceutical dosage form, i.e. magnesium stearate, are mixed and homogeneously blended; the mixture is then compressed to obtain a core which is suitably be provided as tablets obtainable with known tabletting machines. The cores are coated with the coating polymer containing a low water permeable polymer, wherein the coating

polymer composition can comprise additional ingredients, i.e. anti-sticking agents (page 10-12).

**Ascertainment of the difference between the prior art and the claims**

**(MPEP 2141.02)**

Janez et al. do not teach additional ingredient colloidal silicon dioxide is added in the core. However, this deficiency is cured by Seth, P.

Seth, P. teaches a controlled release tablet comprising a core, which comprises venlafaxine, a gelling agent and optional conventional excipient, and a coating; wherein the gelling agent is hydrophilic in nature (i.e. hydroxypropylmethyl cellulose); the other excipients can be lubricant ([0007-0013]). More specifically, Seth, P. teaches a tablet comprising a core formulation, which comprises venlafaxine hydrochloride, hydroxypropylmethyl cellulose and colloidal silicon dioxide ([0039], Example 4).

**Finding of prima facie obviousness Rational and Motivation**

**(MPEP 2142-2143)**

It would have been obvious to a person of ordinary skilled in the art at the time the invention was made to combine the teachings of Janez with Seth to arrive at the claimed invention.

One of ordinary skill in the art would have been motivated to incorporate additional excipients, i.e. colloidal silicone dioxide, because colloidal silicone dioxide is one of the suitable excipients useful in the preparation of solid pharmaceutical dosage

form, and would have been obvious for one of ordinary skill in the art to add to the tablet, if it is desirable, as taught and suggested by the prior art.

From the teaching of the references, one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

**(3) Claims 2, 12-13, 15 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Janez et al. (WO 03/055475) in view of Oosterbaan et al. (WO 03/082805).**

**Applicants Claim**

Applicants claim a controlled release coated tablet comprising: (i) venlafaxine in an amount from 20-60 % by weight; (ii) a hydrophilic polymer, in an amount from 30-70 % by weight, in its core; (iii) a water poorly permeable polymer, in an amount from 1-3 % by weight, in its coating; wherein the hydrophilic polymer comprises a cellulose ester, and the water poorly permeable polymer comprises an acrylic polymer, and wherein the total weight of the tablet does not exceed 500 mg.

**Determination of the scope and content of the prior art**

**(MPEP 2141.01)**

The teaching of Janez et al. has been set forth above.

**Ascertainment of the difference between the prior art and the claims**

**(MPEP 2141.02)**

Janez et al. do not teach the total weight of the tablet does not exceed 500 mg, as claimed. However, this deficiency is cured by Oosterbaan et al.

Oosterbaan et al. teach an extended release pharmaceutical composition in the form of coated tablet comprising venlafaxine salt and hydroxylpropylmethyl cellulose.

Oosterbaan et al. teach that the tablet s can be formulated into any size and shape, such as small or mini-tablets in sizes (page 20, lines 20-31)

**Finding of prima facie obviousness Rational and Motivation**

**(MPEP 2142-2143)**

It would have been obvious to a person of ordinary skilled in the art at the time the invention was made to combine the teachings of Janez and Oosterbaan to arrive at the claimed invention.

One of ordinary skill in the art would have been motivated to substitute the acrylic type polymers: EUDRAGIT RL 30D and/or EUDRAGIT RS 30D taught in Janez with another functional and structural equivalent acrylic type polymer, i.e. EUDRAGIT L30 D, because they all are the acrylic type polymers and all have low water permeability; therefore, they can be used interchangeably for coating purposes.

With respect to the tablet size does not exceed 500 mg as claimed, it would have been obvious to one of ordinary skill in the art for doing so because small or mini tablets containing venlafaxine salt and hydroxypropylmethyl cellulose is known in the art by

Oosterbaan et al., which teaches that such tablets can be formulated into any size and shape. Therefore, one of ordinary skill in the art when reading the references of Janez and Oosterbaan would have been motivated to manufacture the venlafaxine tablet into any size, if it is a desirable or preferred choice to them.

With respect to the recitations where the coated tablet comprises 75 mg of venlafaxine, 100-200 mg of METHOCEL K 100MP and 3-10 mg of EUDRAGIT L30 D-55, although Janez does not exemplify a formulation comprising these constituents: venlafaxine, METHOCEL K 100MP and EUDRAGIT L30 D-55, in said specific amounts; however, Janez suggests that the solid controlled release pharmaceutical formulation comprises a desirable pharmaceutical amount of venlafaxine, i.e. 75 mg or 150 mg; a desirable amount of METHOCEL K100 M Premium, i.e. 70 mg, 150 mg or 250 mg; and a total of 3.5 mg of low water permeable coating polymers (EUDRAGIT RL 30D and EUDRAGIT RS 30D). Therefore, one of ordinary skill in the art when reviewing the reference of Janez would be motivated to try these suggested amounts range, and selects the amount or amount ranges that gives the best, desirable results.

From the teaching of the references, one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

## Conclusion

No claims are allowed.

## Contact Information

Any inquiry concerning this communication from the Examiner should direct to Helen Mei-Ping Chui whose telephone number is 571-272-9078. The examiner can normally be reached on Monday-Thursday (7:30 am – 5:00 pm). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where the application or proceeding is assigned is 571-273-8300.

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